



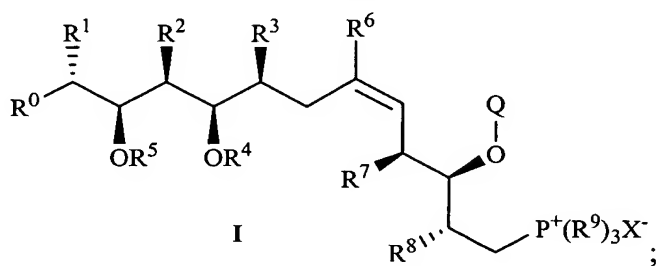
UPN-4377  
Application No.: 10/817,532  
Office Action Dated: March 6, 2006

PATENT

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Original) A process for preparing a compound of formula I:



wherein:

$R^0$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CH_2)_r(C_{3-6}$  cycloalkyl),  $(CH_2)_r$ (aryl) or  $(CH_2)_r$ (heterocycle), wherein  $r$  is selected from 0, 1, 2, 3, and 4;

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$ ,  $R^7$  and  $R^8$  are independently H or  $C_{1-10}$  alkyl;

$R^4$  is an acid labile hydroxyl protecting group;

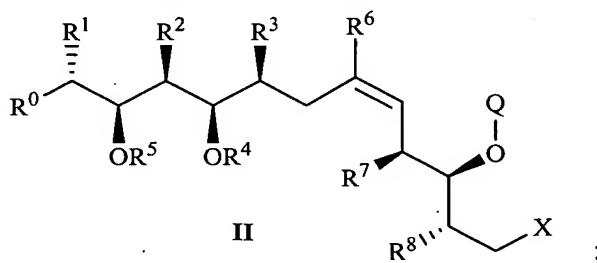
$R^5$  is an oxidatively labile hydroxyl protecting group;

each  $R^9$  is independently  $C_{6-14}$  aryl;

$Q$  is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

$X$  is halogen;

comprising contacting a compound of formula II:



wherein:

$R^0$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CH_2)_r(C_{3-6}$  cycloalkyl),  $(CH_2)_r$ (aryl) or  $(CH_2)_r$ (heterocycle), wherein  $r$  is selected from 0, 1, 2, 3, and 4;

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$ ,  $R^7$  and  $R^8$  are independently H or  $C_{1-10}$  alkyl;

$R^4$  is an acid labile hydroxyl protecting group;

$R^5$  is an oxidatively labile hydroxyl protecting group;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

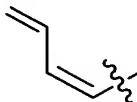
X is halogen;

at a pressure of less than about 10,000 psi with a phosphine of formula  $P(R^9)_3$  wherein each  $R^9$  is independently  $C_{6-14}$  aryl;

for a time and under conditions sufficient to prepare the compound of formula I.

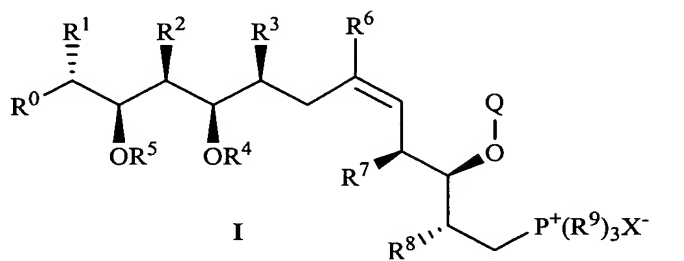
2. (Original) A process according to claim 1 wherein Q is methoxymethyl, methylthiomethyl, 2-methoxyethoxymethyl, acetyl, benzyloxymethyl, 2-(trimethylsilyl)ethoxymethyl or allyl.
3. (Original) A process according to claim 2 wherein Q is methoxymethyl.
4. (Original) A process according to claim 1 wherein the X moiety of the compound of formula II is iodo.
5. (Original) A process according to claim 1 further comprising a base.
6. (Original) A process according to claim 5 wherein the base is non-nucleophilic.
7. (Original) A process according to claim 6 wherein the base is isopropyl-diethylamine.
8. (Original) A process according to claim 1 wherein the reaction is carried out at essentially atmospheric pressure.
9. (Original) A process according to claim 1 wherein  $R^0$  is alkenyl.

10. (Original) A process according to claim 9 wherein R<sup>0</sup> is:



11. (Original) A process according to claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are independently H or C<sub>1-3</sub> alkyl.
12. (Original) A process according to claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>7</sup> and R<sup>8</sup> are methyl and R<sup>3</sup> and R<sup>6</sup> are each independently H or methyl.
13. (Original) A process according to claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are methyl.
14. (Original) A process according to claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>7</sup> and R<sup>8</sup> are methyl and R<sup>6</sup> is H.
15. (Original) A process according to claim 1 wherein the reaction temperature is in the range of about 0 to about 200°C.
16. (Original) A process according to claim 15 wherein the reaction temperature is in the range of about 20 to about 140°C.
17. (Original) A process according to claim 1 wherein the reaction pressure is in the range from about ambient to about 10,000 psi.
18. (Original) A process according to claim 17 wherein the reaction pressure is essentially ambient.
19. (Original) A process according to claim 1 wherein at least one of R<sup>9</sup> is phenyl.
20. (Original) A process according to claim 1 wherein R<sup>5</sup> is *para*-methoxybenzyl.

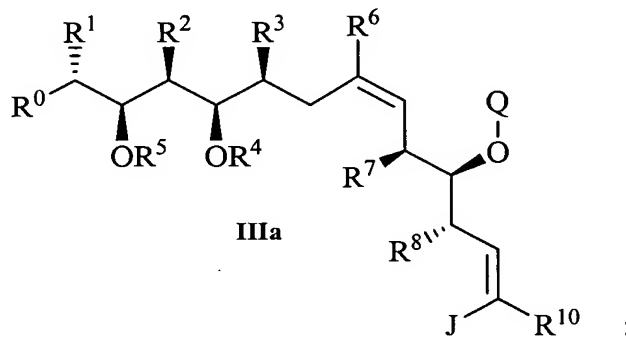
21. (Original) A process according to claim 1 wherein  $R^4$  is  $(R^{16})_3Si-$ , and wherein each  $R^{16}$  is independently  $C_{1-6}$  alkyl.
22. (Original) A process according to claim 21 wherein  $R^4$  is tert-butyldimethylsilyl.
23. (Original) A compound of the formula I:



wherein:

- $R^0$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CH_2)_r(C_{3-6}$  cycloalkyl),  $(CH_2)_r$ (aryl) or  $(CH_2)_r$ (heterocycle), wherein  $r$  is selected from 0, 1, 2, 3, and 4;
- $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$ ,  $R^7$  and  $R^8$  are independently H or  $C_{1-10}$  alkyl;
- $R^4$  is an acid labile hydroxyl protecting group;
- $R^5$  is an oxidatively labile hydroxyl protecting group;
- each  $R^9$  is independently  $C_{6-14}$  aryl;
- $Q$  is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and
- $X$  is halogen.

24. (Original) A process for preparing a compound of formula IIIa:



wherein:

$R^0$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CH_2)_r(C_{3-6}$  cycloalkyl),  $(CH_2)_r$ (aryl) or  $(CH_2)_r$ (heterocycle), wherein  $r$  is selected from 0, 1, 2, 3, and 4;

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$ ,  $R^7$  and  $R^8$  are independently H or  $C_{1-10}$  alkyl;

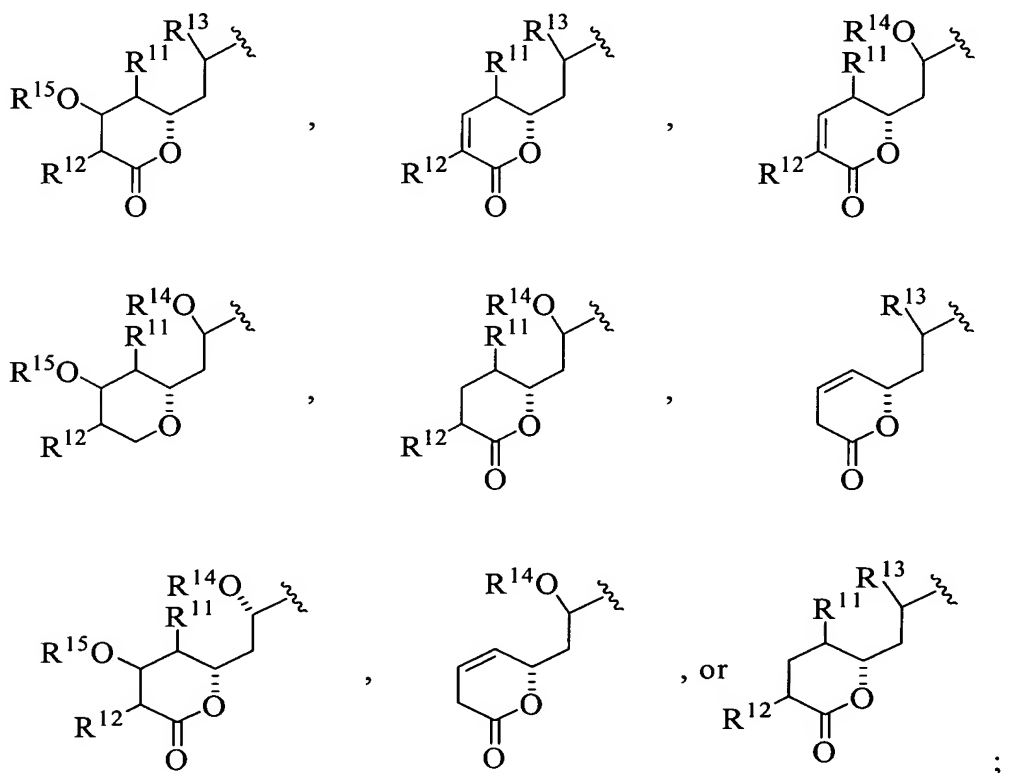
$R^4$  is an acid labile hydroxyl protecting group;

$R^5$  is an oxidatively labile hydroxyl protecting group;

$R^{10}$  is H or  $C_1-C_6$  alkyl;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

J is:

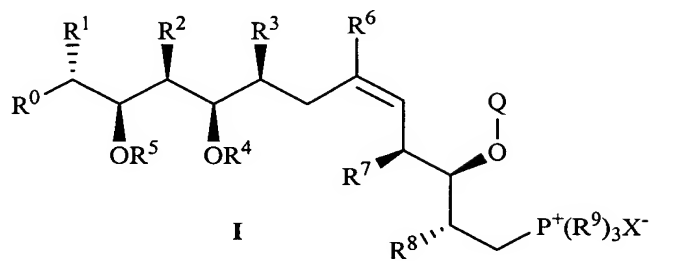


wherein:

$R^{11}$ ,  $R^{12}$  and  $R^{13}$  are each independently H or  $C_1-C_{10}$  alkyl; and

$R^{14}$  and  $R^{15}$  are each independently H or an acid labile hydroxyl protecting group;

comprising contacting a compound of formula I:



wherein:

$R^0$  is  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CH_2)_r(C_{3-6}$  cycloalkyl),  $(CH_2)_r(aryl)$  or  $(CH_2)_r(heterocycle)$ , wherein  $r$  is selected from 0, 1, 2, 3, and

4;

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^6$ ,  $R^7$  and  $R^8$  are independently H or  $C_{1-10}$  alkyl;

$R^4$  is an acid labile hydroxyl protecting group;

$R^5$  is an oxidatively labile hydroxyl protecting group;

$Q$  is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom being protected;

each  $R^9$  is independently  $C_{6-14}$  aryl; and

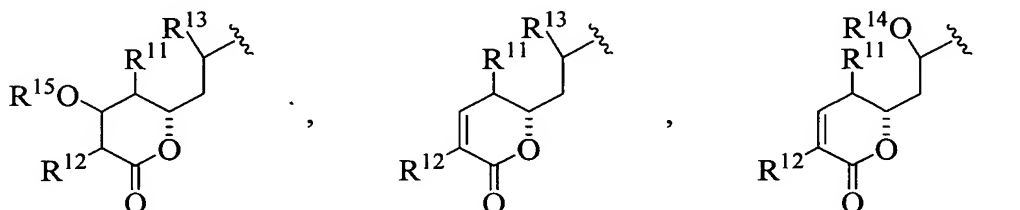
$X$  is halogen;

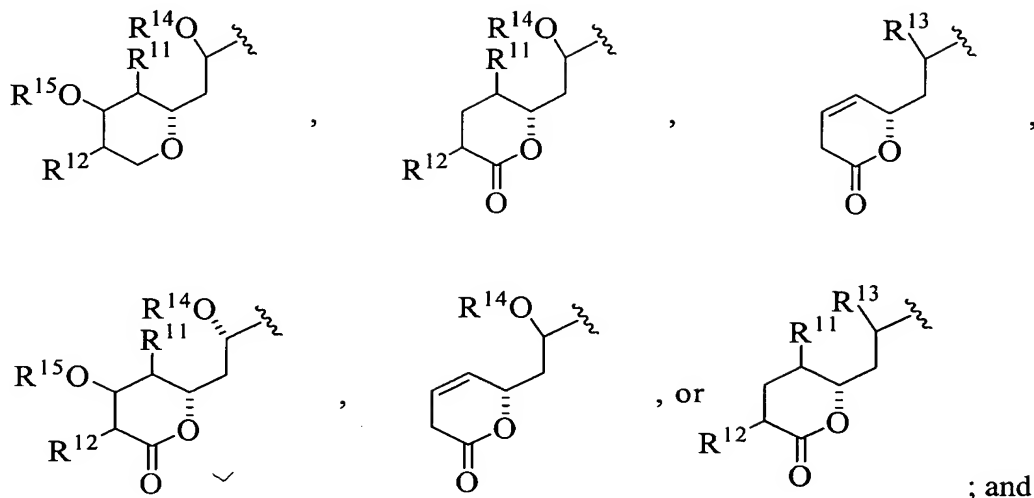
with a compound of formula  $J-C(=O)R^{10}$ ,

wherein:

$R^{10}$  is H or  $C_1-C_6$  alkyl; and

$J$  is:





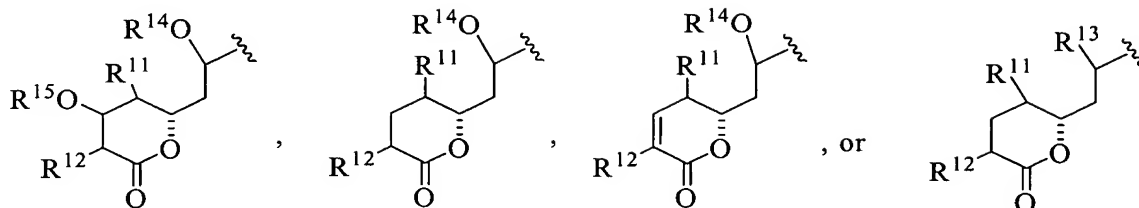
wherein:

$R^{11}$ ,  $R^{12}$ ,  $R^{13}$  and  $R^{16}$  are each independently H or  $C_1$ - $C_{10}$  alkyl; and  
 $R^{14}$  and  $R^{15}$  are each independently H or an acid labile hydroxyl

protecting group;

in the presence of a base for a time and under conditions sufficient to prepare the compound of formula IIIa.

25. (Original) A process according to claim 24, wherein at least one of  $R^{14}$  and  $R^{15}$  is other than H.
26. (Original) A process according to claim 24, wherein the reaction is carried out at a temperature in the range of about  $-30$  to about  $-78^{\circ}\text{C}$ .
27. (Original) A process according to claim 24, wherein the reaction is carried out at a temperature of about  $-78^{\circ}\text{C}$ .
28. (Original) A process according to claim 24, wherein  $R^{10}$  is H.
29. (Original) A process according to claim 24 wherein J is:

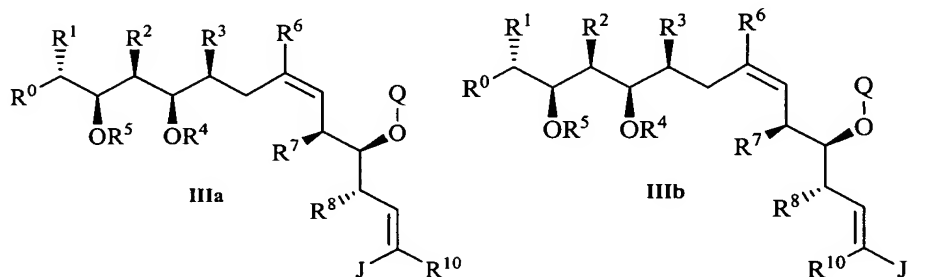


30. (Original) A process according to claim 24, wherein the base is NaHMDS, LiHMDS, KHMDS, MeLi-LiBr complex, n-BuLi (with or without HMPA), KOtBu or NaH.

31. (Original) A process according to claim 30, wherein the base is CH<sub>3</sub>Li-CH<sub>3</sub>Br complex.

32. (Original) A process according to claim 24, wherein the ratio of the compound of formula IIIa to a by-product compound of formula IIIb is at least about 4;

wherein the compounds of formula IIIa and IIIb have the structures:



33. (Original) A process according to claim 32, wherein the ratio of the compound of formula IIIa to the by-product compound of formula IIIb is at least about 10.